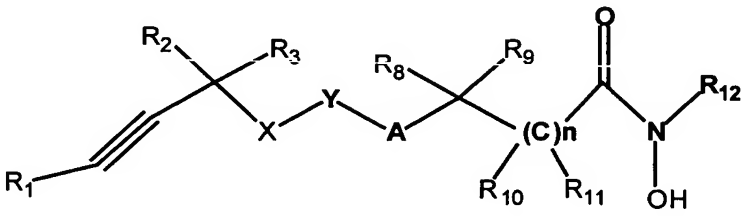
In the Claims

1. A compound of formula



I

wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C4-C8-cycloheteroalkyl;

R_2 and R_3 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R_7 is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R_1, -SO_2-R_1, -C(O)-NHR_1, -$C(O)NR_5R_6$, -$C(O)R_1NR_5R_6$, -C(O)-OR_1, -C(NH)-NH_2.

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

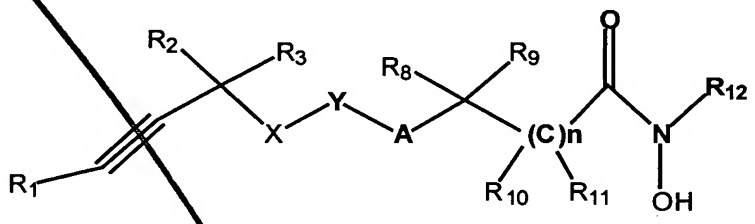
A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

4. A method of inhibiting pathological changes mediated by TNF-α converting enzyme (TACE) in a mammal in need thereof which comprises administering to said mammal a therapeutically effective amount of a compound having the formula



I

wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C_4-C_8-cycloheteroalkyl;

R_2 and R_3 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R_7 is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R_1, -SO_2-R_1, -C(O)-NHR_1, -C(O)NR_5R_6, -C(O)$R_1NR_5R_6$, -C(O)-OR_1, -C(NH)-NH_2.

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C_4-C_8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C_4-C_8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C_4-C_8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

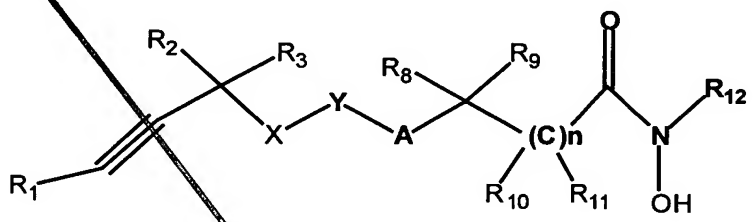
A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof.

6. A pharmaceutical composition comprising a compound having the formula



I

wherein:

R_1 is hydrogen, aryl, heteroaryl, alkyl of 1-8 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, or -C_4-C_8-cycloheteroalkyl;

R_2 and R_3 are each, independently, hydrogen, alkyl of 1-6 carbon atoms, -CN, or -CCH;

R_7 is hydrogen, aryl, aralkyl, heteroaryl, heteroaralkyl, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 1-6 carbon atoms, cycloalkyl of 3-6 carbon atoms, -C(O)-R_1, -SO_2-R_1, -C(O)-NHR_1, -C(O)NR_5R_6, -C(O)$R_1NR_5R_6$, -C(O)-OR_1, -C(NH)-NH_2.

R_8, R_9, R_{10}, and R_{11} are each, independently, hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, alkyl of 1-18 carbon atoms, alkenyl of 2-18 carbon atoms, alkynyl of 2-18 carbon atoms; with the proviso that one of the pairs R8 and R9, R9 and R10 or R10 and R11, together with the carbon atom or atoms to which they are attached, form a cycloalkyl ring of 3-6 carbon atoms, or a -C4-C8-cycloheteroalkyl ring;

R_{12} is hydrogen, aryl or heteroaryl, cycloalkyl of 3-6 carbon atoms, -C4-C8-cycloheteroalkyl, or alkyl of 1-6 carbon atoms;

A is O, S, SO, SO_2, NR_7, or CH_2;

X is O, S, SO, SO_2, NR_7, or CH_2;

Y is aryl or heteroaryl, with the proviso that A and X are not bonded to adjacent atoms of Y; and with the further proviso that if Y is phenyl, then R_8 and R_9 together with the carbon atom to which they are attached may not form a piperdinyl or tetrahydropyranyl ring; and

n is 0-2; or a pharmaceutically acceptable salt thereof;

Please cancel claim 3, without prejudice.

REMARKS

The present application is a divisional of 09/492,686. The specification has been amended to reflect the complete prosecution history. The claims have been amended to delete subject matter which has been allowed in the parent application.

Attached hereto is a marked-up version of the changes made to the application by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."